UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/753,289	01/05/2004	Steven M. Watkins	475512000100	1703

25226 7590 03/24/2008
MORRISON & FOERSTER LLP
755 PAGE MILL RD
PALO ALTO, CA 94304-1018

EXAMINER	
NEGIN, RUSSELL SCOTT	
ART UNIT	**PAPER NUMBER**
1631	

MAIL DATE	DELIVERY MODE
03/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/753,289	WATKINS, STEVEN M.	
	Examiner	Art Unit	
	RUSSELL S. NEGIN	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-17 and 56-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-17 and 56-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Comments

Applicants' amendments and request for reconsideration in the communication filed on 19 December 2007 are acknowledged and the amendments are entered.

Claims 2-17 and 56-59 are pending and examined in the instant Office action.

Withdrawn Rejections

The rejections of claims 2, 3, 5, 6, 12, and 56-58 under 35 U.S.C. 102(b) as being anticipated by Ruan et al. [Journal of Dairy Science, volume 81, 1998, pages 9-15] are withdrawn in view of amendments made to the set of claims on 19 December 2007.

The rejections of claims 15 and 16 under 35 U.S.C. 103(a) as being unpatentable over Ruan et al. as applied above in further view of Moser et al. [Moser et al., Annals of Neurology, volume 45, 1999, pages 100-110] are withdrawn in view of amendments made to the set of claims on 19 December 2007.

The rejections of claims 7, 9, and 13 under 35 U.S.C. 103(a) as being unpatentable over Ruan et al. as applied above in further view of Watkins et al. [Journal of Lipid Research, volume 39, 1998, pages 1583-1588] are withdrawn in view of amendments made to the set of claims on 19 December 2007.

The rejections of claims 4 and 14 under 35 U.S.C. 103(a) as being unpatentable over Ruan et al. as applied above in further view of Watkins et al. in further view of

Siguel [US Patent 5,075,101; IDS of 1/5/2004] are withdrawn in view of amendments made to the set of claims on 19 December 2007.

The rejection of claim 10 under 35 U.S.C. 103(a) as being unpatentable over Ruan et al. as applied above in further view of Grav et al. [Journal of Chromatography B, volume 658, 1994, pages 1-10] is withdrawn in view of amendments made to the set of claims on 19 December 2007.

The rejection of claim 17 under 35 U.S.C. 103(a) as being unpatentable over Ruan et al. as applied above in further view of "The World of Membrane Lipids," [www.biochem.Missouri.edu/~lesa/LIPIDS/membrane_lipid.html; accessed on 6 December 2006, page made on 2 February 1999] is withdrawn in view of amendments made to the set of claims on 19 December 2007.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

<u>The following rejections are newly applied and necessitated by applicant's amendments:</u>

<u>Rejection #1 under 35 U.S.C. 103(a):</u>

Claims 2, 3, 5, 6, 12, and 56-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruan et al. [Journal of Dairy Science, volume 81, 1998, pages 9-15] in view of MacFarlane et al. [Electrophoresis, 1997, volume 18, pages 1796-1806] as evidenced by the definition of "metabolism," (Webster's Ninth New Collegiate Dictionary: 1991, pages 745) and by the definition of metabolite (Mosby's Dictionary of Medicine, Nursing, and Health Professionals, 2006; obtained online at xreferplus.com; 17 March 2008).

Claim 2 is drawn to a method for presenting analysis of quantitative lipid metabolite profiles, comprising:

--designating (a) a first quantitative lipid metabolite profile from a first biological sample and (b) a second quantitative lipid metabolite profile:

--identifying differences or similarities in a plurality of individual lipid metabolites between the first and second quantitative lipid metabolite profiles;

--and displaying the identified differences or similarities on a heat map.

The article of Ruan et al. studies MRI imaging techniques applied to two distinct experiments: water/oil emulsions and cheese block analyses; the abstract of Ruan et al. states:

> Separate magnetic resonance images of water fat of oil-in-water emulsions and cheese blocks were obtained using the chemical shift selective suppression technique. With this technique, the proton signals emitted from water can be readily separated from those emitted from fat in the same sample through a single experiment using magnetic resonance imaging. Relaxation compensation was made to improve the quality of suppression. The experiment using oil-in-water emulsions demonstrated an excellent linear relationship between the intensity of the signal and the concentration of water or fat.

The Materials and Methods section on the second column of page 10 of Ruan et al. elaborates on the procedures of the method described in the abstract:

> ***Oil-in water-emulsions***. Oil in water emulsions were prepared to serve as homogeneous samples for the purpose of development and testing of the MRI techniques. The emulsions were freshly made before the MRI experiments by taking known amounts of vegetable oil (Crisco oil; Proctor & Gamble, Cincinnati, OH) with 3 mM CuSO4 in 20 mm diameter glass tubes… Percentages of oil by volume were 0, 20, 30, 40, 50, 60, 70, and 100%. Three percent of Tween 40 (polyoxyethylene sorbitan monooleate) by volume of the oil was added to improve the stability of the mixture.

Once these oil and water emulsions are made, they are used to generate multiple "lipid metabolite profiles" as explained below.

The definition of lipid metabolic profile on page 8 of the instant specification includes lipids (i.e. oils) as an exemplary embodiment of the term "metabolite."

Additionally, page 9 of the specification shows that lipid profiles are the set of data produces from such a lipid sample.

Additionally, the definitions of metabolism and metabolite in the art states (Webster's Ninth Collegiate Dictionary, Merriam Webster, Inc: 1991, page 745) and (Mosby's Dictionary of Medicine, Nursing and Health Professionals, 2006), respectively:

> Metabolism: The chemical changes in living cells by which energy is provided for vital processes and activities and new material is assimilated.
>
> Metabolite: A substance produced by metabolic action or necessary for a metabolic process. An essential metabolite is one required for a vital metabolic process.

The art shows that vegetable oil (i.e. Crisco) is inherently a metabolite given the definitions of metabolism and metabolite because it is produced by chemical changes in living cells by which new material (i.e. oil) is assimilated.

In the section "Imaging and quantification of water and fat in homogenous fat and water phantoms" on page 12 of Ruan et al., Ruan et al. finds two linear equations corresponding to Figures 5A and 5B, respectively, each of which is interpreted as a "lipid metabolic profile." Figure 5A is the lipid metabolite profile of the oil-in-water

emulsions in a water suppressed MRI image while Figure 5B is the lipid metabolite profile of the same set of oil in water emulsions in a fat suppressed image. Equations 1 and 2 quantify the intensities of the lipid metabolite profiles in Figures 5A and 5B, respectively, to reveal the similarity that the two correlations between the concentration of oil (and water) in the binary mixture and image intensity are linear. The cited definitions and claims do not require each "lipid metabolite profile" to be taken from different sets of samples.

In Figure 5B, the concentration of water is measured because the lipids are suppressed in the image. Water is not a lipid, but in a binary mixture of water and oil, the concentration of water is directly and uniquely dependent on the amount of oil added (the volume of the mixture not occupied by water can only be occupied by oil).

Ruan et al. elaborates on this generation of a plurality metabolite profiles generated from the series of oil in water emulsions described above on page 12, column 2:

> Figure 5 shows a series of water suppressed (A) and fat suppressed (B) magnetic resonance images of the oil-in-water emulsion phantoms. Greater brightness indicates a stronger signal. The signal intensities vary as the water and fat contents vary. When signals that were emitted from water were suppressed (Figure 5A), the signal intensity increased as water content increased. When fat or water was absent from the mixture, little signal can be seen in the water-suppressed or fat-suppressed images, indicating that reliable selective signal suppression was achieved… An excellent linear correlation between the MRI signal intensity and water and fat contents was found.

Figure 5 on page 13 of Ruan et al. illustrates a "heat map" of the fat contents of a variety of different lipid composition profiles. The caption to Figure 5 states, "Magnetic resonance images of oil-in-water phantoms: A. water-suppressed images (the

percentages indicate the oil contents of the mixtures); B. oil-suppressed images (the percentages indicate the water contents of the mixtures)."

Consequently, Ruan et al. shows analysis of multiple lipid mixtures using magnetic resonance imaging, which are designated and mapped in Figure 5 of Ruan et al.

The term "heat map" is not explicitly recited in Ruan et al.

On page 37, lines 17-19, applicant defines heat map as:

> In a heat map display, quantitative metabolite data from a test sample is compared to quantitative metabolite data from a base line or standard sample (a control) and the increase or decrease in each metabolite is indicated on the display, usually in a readily recognizable fashion.

It is inherent that the illustration in Figure 5 of Ruan et al. is a heat map because it is a two dimensional map of multiple lipid profiles marked by shades of colors.

If water is considered the internal standard in measuring lipid concentration, it is inherent that a sample of Crisco vegetable oil comprises lipids that is compared to the standards of 0% lipid content and 100% lipid content in Figure 5 of Ruan et al. (i.e. where the composition of the sample in either all water or without water, respectively).

However, Ruan et al. does not show comparisons of first and second INDIVIDUAL lipid profiles.

The study of Macfarlane et al. develops individual lipoprotein profiles using capillary electrophoresis and mass spectrometry.

Specifically, the bottom panels in Figures 2 and 3 of Macfarlane et al. illustrate electropherograms of two separate lipoproteins (each with an internal standard to calibrate electroosmotic flow).

Claim 3 is further limiting with the additional limitation of the quantitative lipid metabolite profiles comprising quantitative measures of at least two lipids wherein the quantified measurements are obtained using an internal standard for at least one of the lipids.

Figure 5 on page 13 of Ruan et al. illustrates a "heat map" of the fat contents of a variety of different lipid composition profiles. The caption to Figure 5 states, "Magnetic resonance images of oil-in-water phantoms: A. water-suppressed images (the percentages indicate the oil contents of the mixtures); B. oil-suppressed images (the percentages indicate the water contents of the mixtures)."

Consequently, Ruan et al. shows analysis of multiple lipid mixtures using magnetic resonance imaging, which are designated and mapped in Figure 5 of Ruan et al.

Claim 5 is further limiting with the additional limitation that the quantitative lipid metabolite profiles each comprise a quantified measurement of a lipid in a lipid class.

Claim 6 is further limiting wherein the quantified measurement of the lipid in the lipid class is obtained using an internal standard for the lipid class.

Figure 5 of Ruan et al. illustrates the standards at the 0 percent and 100 percent endpoints of Figure in which the mixture is either entirely oil or water to which the linear correlations in the study are applied. (In addition to water, the markers used to measure electroosmotic flow in Macfarlane et al. serve as internal standards.)

Claim 12 is further limiting wherein at least one of the quantitative lipid metabolite profiles is generated comprising separating a biological sample into fractions based on a plurality of lipid classes, wherein at least one quantitative internal standard is included for each lipid class; and measuring the quantity of a plurality of lipid metabolites in the fractions.

Again, Figure 5 of Ruan et al. illustrates the biological samples separated into fractions where water is the standard against which the lipid classes are measured. Additionally, Macfarlane et al. measures individual lipid profiles as discussed above.

Claim 56 is further limiting wherein an increase or decrease in the lipid metabolite is indicated on the heat map by a color and the relevant amount of the increase or decrease is indicated by the intensity of the color.

The “heat maps” in Figure 5 of Ruan et al. illustrate such a trend in colors with respect to lipid content.

Claim 57 is further limiting, further comprising generating a written report.

The figures, tables and equations of Ruan et al. serve as written reports.

Claim 58 is further limiting wherein one of the quantitative lipid metabolite profiles is a control lipomic profile.

In this instance, Figure 5 of Ruan et al. shows the control lipomic profiles at the 100% and 0% levels of each lipid/water.

Claim 59 is further limiting wherein the second quantitative lipid metabolite profile is a lipid metabolite profile from a second biological sample that is different from the first sample.

In this instance the various types of lipoproteins isolated from blood in Macfarlane et al. (i.e. the electropherograms Figures 2-4) serve as the differing lipid metabolite profiles.

It would have been obvious at the time of the instant invention for someone of ordinary skill in the art to modify the heat map analysis of lipids in Ruan et al. by use of the electrophoretic analysis in Macfarlane et al. because it is obvious to substitute known elements to yield a predictable result. In this instance, it would have been obvious to substitute the electrophoretic methods of Macfarlane for the magnetic resonance imaging techniques of Ruan et al. to yield an alternative method of measuring concentration of the lipid. There would have been a reasonable expectation of success in using electrophoresis in place of MRIs because the intensity of the peaks in the electropherograms are also proportional to concentrations of the lipid species.

Response to Arguments:

Applicant's arguments filed 19 December 2007 have been fully considered but they are not persuasive.

Applicant has several arguments regarding this prior art rejection on pages 8-10 of the Remarks.

Applicant first argues that the mixture of Crisco oil in water is not a biological sample. This argument is not persuasive, because given applicant's definition on pages 5-6 of the specification, the definition of "biological sample" contains only exemplary embodiments and encompasses oils obtained from vegetables (i.e. Crisco). In addition, the art shows that vegetable oil is the product of metabolism- i.e. a metabolite (given the standard definitions in the art).

Applicant next argues that Ruan et al. does not teach the amended version of the claim reciting a "plurality of individual lipid profiles." In response the additional reference of Macfarlane et al. is combined with the initial Ruan et al. reference to address this added limitation.

Applicant next argues on page 9 of the Remarks that Ruan et al. does not teach the display of similarities and differences of the lipid profiles on a heat map. This argument is not persuasive because the similarities and differences in color of each of the images themselves serve as the indication of lipid (i.e. oil) concentrations.

With respect to claim 3, applicant argues that an internal standard is not taught because the internal standard has to be internal to the sample itself. This is not persuasive because water is internal to the sample and serves as a standard by which to compare the water/Crisco mixtures when either all water or no water is present.

(Additionally, the Macfarlane reference utilizes the internal standards of electroosmotic flow markers as markers to calibrate a lipid sample with electoosmotic flow in the capillary.)

With respect to claim 5, applicant argues that there is no support in the rejection for any part of this dependent claim. While claim 5 indicates that "quantitative lipid metabolite profiles each comprise a quantified measurement ***of lipid*** in a lipid class," the class of lipid in Crisco oil is vegetable oil. Since claim 5 recite "of lipid" and NOT "of a lipid" the profiles in Ruan et al. serve to describe the teachings of this claim.

With respect to claims 6 and 12, applicant next argues that no "internal standard" is taught. For the reasons described in the arguments against instant claim 3, the applicant's arguments for this claim are also not persuasive. With respect to claim 12, applicant additionally argues the "individual lipid profiles" in the amended claim is not taught in Ruan et al. For this reason, the article of Macfarlane et al. is combined with the initial study of Ruan et al. Applicants additionally argue with regards to claim 12 that the Ruan et al. reference does not teach that the 100% oil or water samples were derived from a mixture. This is not persuasive because claim 12 nowhere recites that the samples are derived from mixtures.

With respect to claim 58, applicants argue that Ruan et al. does not teach the use of a control lipomic profile. Absent a definition of "control lipomic profile" in the specification, the lipomic profile in Ruan et al. is interpreted to be a control lipomic profile.

Rejection #2 under 35 U.S.C. 103(a):

Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruan et al. in view of Macfarlane et al. as applied to claims 2, 3, 5, 6, 12, and 56-59 above as evidenced by the definition of “metabolism” and “metabolite" in further view of Moser et al. [Moser et al., Annals of Neurology, volume 45, 1999, pages 100-110].

Claims 15 and 16 are further limiting wherein the separating and measuring methods comprise chromatography.

Ruan et al. and Macfarlane et al. make obvious a comparative profile of lipid concentrations, as discussed above.

Ruan et al. and Macfarlane et al. do not teach chromatography.

The study of Moser et al., entitled, “Plasma very long chain fatty acids in 3,000 peroxisome disease patients and 29,000 controls,” states in the first sentence of the abstract, “The assay of plasma very long chain fatty acids (VLCFAs), developed in our laboratory on 1981, has become the most widely used procedure for the diagnosis of X-linked adrenoleukodystrophy (X-ALD) and other peroxisomal disorders.”

The second column of page 101 of Moser et al. (Neurology) states:

> *Capillary Gas Liquid Chromatographic Analysis of Very Long Chain Fatty Acids*
> The VLCFA assay procedure was described in 1981 and modified in 1991. Recently we have introduces a two-column procedure that permits quantitation of 65 fatty acids. All three procedures give identical results for three measurements that are the topic of the present report.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the lipid composition studies of Ruan et al. and Macfarlane et al. by use of the chromatographic analysis of Moser et al., wherein the motivation would have been that while the aforementioned studies quantify lipids, Moser

et al. has the advantage of using chromatographic analysis of lipids to specifically address peroxisomal disorders (see abstract of Moser et al.).

Response to arguments:

Applicant's arguments filed 19 December 2007 have been fully considered but they are not persuasive.

Applicants have no arguments that are specific to this rejection, and the arguments that pertain to the Ruan et al. reference are discussed above.

Rejection #3 under 35 U.S.C. 103(a):

Claims 7, 9, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruan et al. in view of Macfarlane et al. above as evidenced by the definitions of “metabolism” and “metabolite" as applied to claims 2, 3, 5, 6, 12, and 56-59 above in further view of Watkins et al. [Journal of Lipid Research, volume 39, 1998, pages 1583-1588].

Claim 7 is further limiting with the additional limitation of requiring linoleic acid (18:2n6).

Claim 9 is further limiting with the additional limitation of requiring cardiolipins.

Claim 13 is further limiting with the additional limitation of requiring cardiolipins.

Ruan et al. and Macfarlane et al. make obvious a comparative profile of lipid concentrations, as discussed above.

Ruan et al. and Macfarlane do not teach use of cardiolipins and specifically the linoleic acid 18:2 n-6.

The study of Watkins et al., entitled, "Docosahexaxenoic acid accumulates in cardiolipin and enhances HT-29 cell oxidant production," states in the first sentence of the abstract, "The objective of this study was to investigate membrane fatty acids for their effects on mitochondrial function in live cells."

The top of column 2 of page 1583 details some of the specific lipid studied, as stated, "In mammals, CL acyl composition is unusually sensitive to diet, and in humans it is rich in the essential fatty acid linoleic acid (LA, 18:2 n-6)."

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the lipid composition study of Ruan et al. and Macfarlane et al. by use of the cardiolipin study of Watkins et al., wherein the motivation would have been that while Ruan et al. and Macfarlane et al. quantify lipids, Watkins et al. has the advantage of quantifying cardiolipins in mitochondria for the purpose of understanding oxidant production and aging (see abstract of Watkins et al.).

Response to arguments:

Applicant's arguments filed 19 December 2007 have been fully considered but they are not persuasive.

Applicants have no arguments that are specific to this rejection, and the arguments that pertain to the Ruan et al. reference are discussed above.

Rejection #4 under 35 U.S.C. 103(a):

Claims 4 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruan et al. in view of Macfarlane et al. in view of Watkins et al. as evidenced by the definitions of "metabolism" and "metabolite" as applied to claims 2, 3, 5, 6, 7, 9, 12, 13, and 56-59 above in further view of Siguel [US Patent 5,075,101; IDS of 1/5/2004].

Claims 4 and 14 are further limiting, limiting the metabolites to ***5,8,11-eicosatrienoic acid, 5,8,11,14,17-eicosapentaenoic acid, 5,8,11-eicosatrienoic acid, and 5,8,11,14,17-eicosapentaenoic acid.***

Ruan et al., Macfarlane et al., and Watkins et al., make obvious the method of fatty acid analysis, as discussed above.

However, these three sources do not teach the specific molecules of the claims, including the above mentioned 5,8,11-eicosatrienoic acid (Mead acid).

The patent of Siguel, entitled, "Method of diagnosis of fatty acid or lipid abnormalities," states in column 3, lines 55-65, that Mead acid is an essential fatty acid important in preventing essential fatty acid deficiency.

It would have been obvious for someone of ordinary skill in the art at the time of the instant invention to modify the lipid mixture analyses of Ruan et al., Macfarlane et al., and Watkins et al. by the use of Mead acid in Siguel wherein the motivation would have been that Siguel shows the advantage of Mead acid in that adequate amounts of Mead acid are required to prevent lipid deficiency in the blood [see column 3, lines 55-65 of Siguel].

Response to arguments:

Applicant's arguments filed 19 December 2007 have been fully considered but they are not persuasive.

Applicants have no arguments that are specific to this rejection, and the arguments that pertain to the Ruan et al. reference are discussed above.

Rejection #5 under 35 U.S.C. 103(a):

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ruan et al. in view of Macfarlane above as evidenced by the definitions of "metabolism" and "metabolite" applied to claims 2, 3, 5, 6, 12, and 56-59 above in further view of Dutta et al. [JAOCS, volume 74, no. 6, 1997, pages 647-657].

Claim 8 is further limiting the types of sterols to be employed as lipids.

Ruan et al. and Macfarlane et al. make obvious a comparative profile of lipid concentrations, as discussed above.

Ruan et al. and Macfarlane et al. do not teach use of cholestan-3b-ols.

The article of Dutta et al., entitled, "Studies of phytosterol oxides: I: Effect of storage on the content in potato chips prepared in different vegetable oils," states in the abstract:

> Potato chips fried in palm oil, sunflower oil, and high-oleic sunflower oil were studies for the content of different phytosterol oxides during 0 to 25 weeks of storage in the dark. Oxidation products of sitosterol (2,4 alpha-ethyl-5-cholesten-2b-ol) and campesterol (2,4 alpha methyl-5cholesten-3b-ol) were synthesized to help identify the phytesterol oxides.

Dutta et al. continue in the introduction to explain in the first sentence of the introduction:

> Abundant information exists on the formation of cholesterol oxidation products in foods and their biological implications, but there is relatively little on such products generated from phytosterols.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the lipid quantification method of Ruan et al. and Macfarlane et al. by use of the phytosterol quantitation method of Dutta et al. wherein the motivation would have been that the study of Dutta et al. has the advantage of using the required fatty acids for further understanding of biological implications of cholesterols and phytosterols (see introduction of Dutta et al. on page 647).

Response to arguments:

Applicant's arguments filed 19 December 2007 have been fully considered but they are not persuasive.

Applicants have no arguments that are specific to this rejection, and the arguments that pertain to the Ruan et al. reference are discussed above.

Rejection #6 under 35 U.S.C. 103(a):

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ruan et al. in view of Macfarlane et al. above as evidenced by the definition of “metabolism” and “metabolite” as applied to claims 2, 3, 5, 6, 12, and 56-59 above in further view of Grav et al. [Journal of Chromatography B, volume 658, 1994, pages 1-10].

Claim 10 is further limiting in the types of internal standards to be employed.

Ruan et al. and Macfarlane et al. make obvious a comparative profile of lipid concentrations, as discussed above.

Ruan et al. and Macfarlane et al. do not teach the specific internal standards to be used.

The article of Grav et al., entitled, "Gas chromatographic measurement of 3- and 4-thia fatty acids incorporated into various classes of rat liver lipids during feeding experiments," states in the first sentence of the abstract, "A practical procedure is described for the quantitative measurement of the amount of acyl units derived from tetradecylthioacetic acid (effecting hypolipemia in rats) and tetradecylthiopropionic acid (effecting hyperlipemia)."

The abstract of Grav et al. continues, "The overall recoveries of heptadecanoyl lipids added as internal standards using extraction were 94% to 96%, except for cholesteryl heptadecanoate…"

In Grav et al., section 2.3 on page 2, Grav et al. disclose that one of the species used in claim 10, diheptadecanoyl phosphatidylcholine is used as an internal standard.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the lipid quantification method of Ruan et al. and Macfarlane et al. by use of the use of the specific standards of Grav et al. wherein the motivation would have been that while Grav et al. disclose a method of quantifying lipids in livers, Grav et al. has the advantage of using the required internal standards in a direct health application in examining hypolipemia and hyperlipemia (see abstract of Grav et al.).

Response to arguments:

Applicant's arguments filed 19 December 2007 have been fully considered but they are not persuasive.

Applicants have no arguments that are specific to this rejection, and the arguments that pertain to the Ruan et al. reference are discussed above.

Rejection #7 under 35 U.S.C. 103(a):

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ruan et al. in view of Macfarlane et al. above as evidenced by the definition of "metabolism" and "metabolite" as applied to claims 2, 3, 5, 6, 12, and 56-59 above in further view of "The World of Membrane Lipids," [www.biochem.Missouri.edu/~lesa/LIPIDS/membrane_lipid.html; accessed on 6 December 2006, page made on 2 February 1999].

Claim 17 is further limiting wherein displaying generates a web page for viewing.

Ruan et al. and Macfarlane et al. make obvious a comparative profile of lipid concentrations, as discussed above.

However, Ruan et al. and Macfarlane et al. do not teach the use of a web page for electronically displaying of results.

"The World of Membrane Lipids," states in its introduction:

> This website is an unofficial home for membrane lipid crystal structures. Here, you'll be able to find information about the nomenclature, crystallization, etc. of membrane lipids. Although about 50 structures are known, most of them are not in a database, so the only source of their coordinates is the original journal article.
> The purpose of this site is to make this information available to anyone interested, especially structural biologists. To facilitate their use, all coordinate files are in PDB format. If you have any comments or contributions, please send them to Lesa Beamer.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the lipid quantification method of Ruan et al. and Macfarlane et al. by use of the web posting database of "The World of Membrane Lipids," wherein the motivation would have been that posting lipid results on a web page has the advantage of making the data available to the general public (see introduction of "The World of Membrane Lipids").

Response to arguments:

Applicant's arguments filed 19 December 2007 have been fully considered but they are not persuasive.

Applicants have no arguments that are specific to this rejection, and the arguments that pertain to the Ruan et al. reference are discussed above.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/RSN/
17 March 2008

/Marjorie Moran/
Supervisory Patent Examiner, Art Unit 1631